Answer 1:

Bibliographic Information

Cytidine triphosphate synthetase (CTP synthetase) as a druggable target in cancer. Verschuur, Arnauld C. Pediatric Oncology Department, Emma Children's Hospital, University of Amsterdam, Amsterdam, Neth. Drugs of the Future (2007), 32(12), 1071-1080. Publisher: Prous Science, CODEN: DRFUD4 ISSN: 0377-8282. Journal; General Review written in English. CAN 148:393577 AN 2008:216937 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A review. Cytidine triphosphate (CTP) synthetase is a key enzyme in the biosynthesis of pyrimidine ribonucleotides. The enzyme catalyzes the conversion of uridine triphosphate (UTP) to CTP and is the predominant pathway for the synthesis of CTP in proliferating and malignant tissues. Elevated CTP synthetase activity is seen in various malignancies, such as acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), hepatoma, colon cancer and renal carcinoma, as well as non-Hodgkin's lymphoma (NHL). The high activity of the enzyme has led to the development of inhibitors as potential new therapeutic tools. The best explored inhibitor of CTP synthetase is cyclopentenyl cytosine (CPEC), which has been investigated in both preclin. and clin. studies. CPEC proved to profoundly inhibit CTP synthetase in vitro in colon carcinoma, ALL and AML cell lines. Moreover, CPEC has been shown to inhibit the growth of human and murine leukemia xenografts in vivo. A phase I clin. trial with CPEC as monotherapy showed that this compd. inhibits CTP synthetase in surrogate tissues such as bone marrow. However, at the highest doses, CPEC proved to have severe cardiovascular toxicity, the mechanism of which has not been unraveled until recently. Addnl. preclin. studies did not show any cardiotoxicity in rats. There is probably a good rationale for using CPEC at lower doses, since it has been shown in preclin. models to display synergistic cytotoxic effects with other nucleoside analogs such as cytarabine or gemcitabine. In conclusion, CTP synthetase is a druggable target, esp. for combination treatment of AML and ALL.

Answer 2:

Bibliographic Information

Synergistic antileukemic effects between ABT-869 and chemotherapy involve downregulation of cell cycle-regulated genes and c-Mos-mediated MAPK pathway. Zhou, J.; Pan, M.; Xie, Z.; Loh, S.-L.; Bi, C.; Tai, Y.-C.; Lilly, M.; Lim, Y.-P.; Han, J.-H.; Glaser, K. B.; Albert, D. H.; Davidsen, S. K.; Chen, C.-S. Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore. Leukemia (2008), 22(1), 138-146. Publisher: Nature Publishing Group, CODEN: LEUKED ISSN: 0887-6924. Journal written in English. CAN 149:118833 AN 2008:64902 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Internal tandem duplications (ITDs) of fms-like tyrosine kinase 3 (FLT3) receptor play an important role in the pathogenesis of acute myeloid leukemia (AML) and represent an attractive therapeutic target. ABT-869 has demonstrated potent effects in AML cells with FLT3-ITDs. Here, we provide further evidence that ABT-869 treatment significantly downregulates cyclins D and E but increases the expression of p21 and p27. ABT-869 induces apoptosis through downregulation of Bcl-xL and upregulation of BAK, BID and BAD. We also evaluate the combinations of ABT-869 and chemotherapy. ABT-869 demonstrates significant sequence-dependent synergism with cytarabine and doxorubicin in cell lines and primary leukemia samples. The optimal combination was validated in MV4-11 xenografts. Low-d. array anal. revealed the synergistic interaction involved in downregulation of cell cycle and mitogen-activated protein kinase pathway genes. CCND1 and c-Mos were the most significantly inhibited targets on both transcriptional and translational levels. Treatment with short hairpin RNAs targeting either CCND1 or c-Mos further sensitized MV4-11 cells to ABT-869. These findings suggest that specific pathway genes were further targeted by adding chemotherapy and support the rationale of combination therapy. Thus, a clin. trial using sequence-dependent combination therapy with ABT-869 in AML is warranted.

Answer 3:

Bibliographic Information

Clinical and mechanistic aspects of glucocorticoid-induced chemotherapy resistance in the majority of solid tumors. Zhang, Chengwen; Wenger, Till; Mattern, Juergen; Ilea, Septimia; Frey, Christian; Gutwein, Paul; Altevogt, Peter; Bodenmueller, Wolfram; Gassler, Nikolaus; Schnabel, Philipp A.; Dienemann, Hendrik; Marme, Alexander; Hohenfellner, Markus; Haferkamp, Axel; Pfitzenmaier, Jesco; Groene, Hermann-Josef; Kolb, Armin; Buechler, Peter; Buechler, Markus W.; Friess, Helmut; Rittgen, Werner; Edler, Lutz; Debatin, Klaus-Michael; Krammer, Peter H.; Rutz, Hans P.; Herr, Ingrid. Research Group Molecular OncoSurgery, University of Heidelberg, Heidelberg, Germany. Cancer Biology & Therapy (2007), 6(2), 278-287. Publisher: Landes Bioscience, CODEN: CBTAAO ISSN: 1538-4047. Journal written in English. CAN 147:479951 AN 2007:1039338 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Glucocorticoids have been used widely in conjunction with cancer therapy due to their ability to induce apoptosis in hematol. cells and to prevent nausea and emesis. However, recent data including ours, suggest induction of therapy-resistance by glucocorticoids in solid tumors, although it is unclear whether this happens only in few carcinomas or is a more common cell type specific phenomenon. We performed an overall statistical anal. of our new and recent data obtained with 157 tumor probes evaluated in vitro, ex vivo and in vivo. The effect of glucocorticoids on apoptosis, viability and cell cycle progression under diverse clin. important questions was examd. New in vivo results demonstrate glucocorticoid-induced chemotherapy resistance in xenografted prostate cancer. In an overall statistical anal. we found glucocorticoid-induced resistance in 89% of 157 analyzed tumor samples. Resistance is common for several cytotoxic treatments and for several glucocorticoid-derivs. and due to an inhibition of apoptosis, promotion of viability and cell cycle progression. Resistance occurred at clin. achievable peak plasma levels of patients under anti-emetic glucocorticoid therapy and below, lasted for a long time, after one single dose, but was reversible upon removal of glucocorticoids. Two nonsteroidal alternative anti-emetic agents did not counteract anticancer treatment and may be sufficient to replace glucocorticoids in cotreatment of carcinoma patients. These data demonstrate the need for prospective clin. studies as well as for detailed mechanistic studies of GC-induced cell-type specific pro- and anti-apoptotic signaling.

Answer 4:

Bibliographic Information

Synergistic antileukemia effect of genistein and chemotherapy in mouse xenograft model and potential mechanism through MAPK signaling. [Erratum to document cited in CA147:133146]. Shen, Jing; Tai, Yan-Chin; Zhou, Jian-biao; Wong, Ching-Ho Stephen; Cheang, Pek Tan S.; Wong, Wai-Shiu Fred; Xie, Zhigang; Khan, Matiullah; Han, Jin-Hua; Chen, Chien-Shing. Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore. Experimental Hematology (New York, NY, United States) (2007), 35(5), 854. Publisher: Elsevier Inc., CODEN: EXHMA6 ISSN: 0301-472X. Journal written in English. CAN 147:203256 AN 2007:871383 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

On page 75, in the bottom left column, offprint requests was given incorrectly, and should read: "Offprint requests to: Jin-Hua Han, Ph.D., Department of Biological Sciences, National University of Singapore, 14 Science Drive 4, Singapore 117543; E-mail: jinhuahan@nus.edu.sg".

Answer 5:

Bibliographic Information

A Novel FLT3 Inhibitor FI-700 Selectively Suppresses the Growth of Leukemia Cells with FLT3 Mutations. Kiyoi, Hitoshi; Shiotsu, Yukimasa; Ozeki, Kazutaka; Yamaji, Satomi; Kosugi, Hiroshi; Umehara, Hiroshi; Shimizu, Makiko; Arai, Hitoshi; Ishii, Kenichi; Akinaga, Shiro; Naoe, Tomoki. Department of Infectious Diseases, Nagoya University School of Medicine, Japan. Clinical Cancer Research (2007), 13(15, Pt. 1), 4575-4582. Publisher: American Association for Cancer Research, CODEN: CCREF4

ISSN: 1078-0432. Journal written in English. CAN 149:118806 AN 2007:835998 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

PURPOSE: The aim of this study was to evaluate the antileukemia activity of a novel FLT3 kinase inhibitor, FI-700. Exptl. Design: The antileukemia activity of FI-700 was evaluated in human leukemia cell lines, mutant or wild-type (Wt)-FLT3-expressing mouse myeloid precursor cell line, 32D and primary acute myeloid leukemia cells, and in xenograft or syngeneic mouse leukemia models. RESULTS: FI-700 showed a potent IC50 value against FLT3 kinase at 20 nmol/L in an in vitro kinase assay. FI-700 showed selective growth inhibition against mutant FLT3-expressing leukemia cell lines and primary acute myeloid leukemia cells, whereas it did not affect the FLT3 ligand (FL)-driven growth of Wt-FLT3-expressing cells. These antileukemia activities were induced by the significant dephosphorylations of mutant FLT3 and STAT5, which resulted in G1 arrest of the cell cycle. Oral administration of FI-700 induced the regression of tumors in a s.c. tumor xenograft model and increased the survival of mice in an i.v. transplanted model. Furthermore, FI-700 treatment eradicated FLT3/ITD-expressing leukemia cells, both in the peripheral blood and in the bone marrow. In this expt., the depletion of FLT3/ITD-expressing cells by FI-700 was more significant than that of Ara-C, whereas bone marrow suppression by FI-700 was lower than that by Ara-C. CONCLUSIONS: FI-700 is a novel and potent FLT3 inhibitor with promising antileukemia activity.

Answer 6:

Bibliographic Information

Synergistic antileukemia effect of genistein and chemotherapy in mouse xenograft model and potential mechanism through MAPK signaling. Shen, Jing; Tai, Yan-Chin; Zhou, Jian-biao; Wong, Ching-Ho Stephen; Cheang, Pek Tan S.; Wong, Wai-Shiu Fred; Xie, Zhigang; Khan, Matiullah; Han, Jin-Hua; Chen, Chien-Shing. Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore. Experimental Hematology (New York, NY, United States) (2007), 35(1), 75. Publisher: Elsevier Inc., CODEN: EXHMA6 ISSN: 0301-472X. Journal written in English. CAN 147:133146 AN 2007:15648 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

We investigated the antiproliferative effect of genistein, and its antileukemia effect in combination with cytosine arabinoside (ara-C) in acute myeloid leukemia (AML). Optimal dosage of genistein as single agent and in combination with ara-C was first detd. in vitro. Genistein demonstrated a dose- and time-dependent inhibition of cell proliferation, induction of apoptosis, and cell-cycle arrest at G2/M phase. Gene-expression profiles revealed mitogen-activated protein kinase (MAPK) signaling as one of the most affected biol. pathways. Phosphatidylinositol 3 kinase, protein kinase A, protein kinase C, MAPK kinase 4, KIT, PIM1, and transforming growth factor-β receptor 1, were significantly downregulated by genistein. To test whether genistein could augment the antiproliferation activity of ara-C, 2 groups of severe combined immunodeficient mice were inoculated with NB4 and HL-60 cells, resp., followed by treatment with either genistein or combination of genistein and ara-C. The combination treatment significantly inhibited tumor growth, and improved survival of NB4 ($p = 0.0031$) and HL-60 ($p = 0.0007$) xenograft mice. Our present study highlighted the schedule-dependent synergistic antileukemia effect of genistein with chemotherapy in both in vitro and in vivo models. This novel combination could potentially be a promising regimen for treatment of AML.

Answer 7:

Bibliographic Information

Incorporation of OSI-7836 into DNA of Calu-6 and H460 xenograft tumors. Richardson, Frank; Black, Chris; Richardson, Katherine; Franks, April; Wells, Edward; Karimi, Susan; Sennello, Gina; Hart, Karen; Meyer, Denny; Emerson, David; Brown, Eric; LeRay, Jeremy; Nilsson, Christy; Tomkinson, Blake; Bendele, Raymond. OSI Pharmaceuticals, Inc., Boulder, CO, USA. Cancer Chemotherapy and Pharmacology (2005), 55(3), 213-221. Publisher: Springer GmbH, CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 142:329107 AN 2005:10437 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

OSI-7836 (4'-thio-β-d-arabinofuranosylcytosine) is a novel nucleoside analog in phase I clin. development for the treatment of cancer. As with other nucleoside analogs, the proposed mechanism of action involves phosphorylation to the triphosphate form followed by incorporation into cellular DNA, leading to cell death. This hypothesis has been examd. by measuring and comparing the incorporation of ara-C, OSI-7836, and gemcitabine (dFdC) into DNA of cultured cells and by investigating the role of deoxycytidine kinase in OSI-7836 toxicity. We report here addnl. studies in which the role of cell cycling on OSI-7836 toxicity was investigated and incorporation of OSI-7836 into DNA of xenograft tumors measured. The role of the cell cycle was examd. by comparing the toxicity of OSI-7836 in A549 NSCLC cells that were either in log phase growth or had reached confluence. A novel validated LC-MS/MS assay was developed to quantify the concns. of OSI-7836 in DNA from Calu-6 and H460 human tumor xenografts in mice. Results showed that apoptosis induced by OSI-7836 was markedly greater in cycling cells than in confluent non-cycling cells despite only a modest increase in intracellular OSI-7836 triphosphate concn. The LC-MS/MS assay developed to measure OSI-7836 incorporation into DNA had an on-column detection limit of 0.25 fmol, a quantification limit of 0.5 fmol, and a sensitivity of approx. 0.1 pmol OSI-7836/μmol dThy. Concns. of OSI-7836 in splenic DNA (0.4 pmol OSI-7836/μmol dThy) averaged fivefold less than the av. concn. in Calu-6 and H460 xenograft DNA (3.0 pmol OSI-7836/μmol dThy) following a 400 mg/kg dose of OSI-7836. Concns. of OSI-7836 in Calu-6 tumor DNA isolated 24 h following a dose of 400, 1000, or 1600 mg OSI-7836/kg were approx. 1.3, 1 and 1.3 pmol OSI-7836/μmol dThy, resp. Concns. of OSI-7836 in DNA from H460 and Calu-6 xenografts did not appear to increase during repeated administration of 400 mg OSI-7836/kg on days 1, 4, 7, and 10.

The majority of OSI-7836 in DNA from Calu-6 and H460 tumors of mice dosed with 1600 mg/kg was located at internal nucleotide linkages, similar to dFdC and ara-C. In conclusion, cell cycling studies supported the hypothesis that OSI-7836 cytotoxicity is dependent upon DNA synthesis. A validated LC-MS/MS assay was developed that could quantify OSI-7836 in DNA from tissues. The assay was used to show that OSI-7836 was incorporated in internal linkages in tumor DNA in a manner that was dose-independent at the doses tested and did not appear to accumulate during repeated dosing. The results suggest that if DNA incorporation is a toxic event, the relationships between administered dose, DNA incorporation, and toxicity are complex.

Answer 8:

Bibliographic Information

Predictability of clinical response to anticancer agents in human cancer xenografts. Tsukamoto, Fumine. Med. Sch., Osaka Univ., Suita, Japan. Osaka Daigaku Igaku Zasshi (1994), 46(4), 251-61. CODEN: ODIZAK ISSN: 0369-710X. Journal written in Japanese. CAN 121:124753 AN 1994:524753 CAPLUS

Abstract

Nude mouse transplanted human tumors retained original sensitivity to antitumor drugs, and was useful in secondary screening for the sensitivity to tumor chemotherapy. Fresh tumor tissues were transplanted and maintained in nude mice in 77 cases (tried: 247 cases), and sensitivity of the transplanted tumors to chemotherapy was compared between human therapy and in nude mice using regimen used clin. in 17 cases with 21 expts. (stomach, breast, colon, pancreas, esophagus. melanoma). Tested drugs were adriamycin, cisplatin, cyclophosphamide, cytarabine, dacarbazine, doxifluoridine, epirubicin, 5-fluorouracil, M-83 (a mitomycin C deriv.), mitomycin C, tegafur, and UFT. Chemotherapy in nude mice was effective in 6 expts., which coincided with clin. results in 5 cases. The ineffective 15 cases in nude mice coincided with the clin. results in all cases.

Answer 9:

Bibliographic Information

Xenografts in pharmacologically immunosuppressed mice as a model to test the chemotherapeutic sensitivity of human tumors. Floersheim, G. L.; Bieri, A.; Chiodetti, Nicole. Zent. Lehre Forsch., Kantonssp., Basel, Switz. International Journal of Cancer (1986), 37(1), 109-14. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 104:81665 AN 1986:81665 CAPLUS

Abstract

A human tumor xenograft model using pharmacol. immunosuppressed mice was assessed for its suitability to test preclinically the sensitivity of colorectal carcinomas, bone sarcomas and melanomas against anticancer agents. Beside ionizing radiation, 14 cytotoxic drugs including 5-fluorouracil (5-FU) [51-21-8], dimethylmyleran (DMM) [55-93-6], cytosine arabinoside [147-94-4], cyclophosphamide [50-18-0], melphalan [148-82-3], mitomycin C [50-07-7], adriamycin [23214-92-8], bleomycin [11056-06-7], etoposide [33419-42-0], vinblastine [865-21-4], cisplatin [15663-27-1], procarbazine [671-16-9], DTIC [4342-03-4], and BCNU [154-93-8] were assayed. Ionizing radiation, 5-FU and DMM were also applied at LDs followed by bone-marrow rescue high-dose therapy. Four colon carcinomas responded poorly to most of the agents but one tumor displayed marked sensitivity to BCNU. LDs of radiation, 5-FU and DMM and cyclophosphamide and by an osteosarcoma to the latter drug. No strong effects were seen against melanomas. LDs of DMM induced the best regression of one colon carcinoma. In general, the superiority of high-dose therapy for solid human tumors compared to maximally tolerated doses was demonstrated. Individual carcinomas of the same type displayed different drug sensitivity.

Answer 10:

Bibliographic Information

Screening test of antitumor agents by human tumor cell lines in nude mice in ascitic form. Kitahara, Takeshi; Minato, Keisuke; Shimoyama, Masanori. Natl. Cancer Cent. Hosp., Japan. Gan no Rinsho (1984), 30(9), 1158-67. CODEN: GANRAE ISSN: 0021-4949. Journal written in Japanese. CAN 102:17008 AN 1985:17008 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Human breast cancer and leukemic cells implanted in nude mice appeared to be useful models for the screening of neoplasm inhibitors. The sensitivities of implanted tissues to drugs were similar to those found in patients. Studies on the suitable route of administration in these mice provide the best administration routes for humans.

Answer 11:

Bibliographic Information

Comparative data from experimental chemotherapy of human tumor xenografts in nude mice, and the clinical responses of the patient-donors. Taguchi, Tetsuo; Fujita, Masahide. Univ. Osaka, Osaka, Japan. Eksperimental'naya i Klinicheskaya Farmakoterapiya (1983), 12 77-83. CODEN: EKFMA7 ISSN: 0367-0589. Journal written in Russian. CAN 100:167828 AN 1984:167828 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A high degree of correlation was found between the effects of ftorafur [17902-23-7] in combination with MFC (mitomycin C [50-07-7], 5-fluorouracil [51-21-8], and cytosine arabinoside [147-94-4]) on the growth of tumor xenografts of 3 different human tumors in nude mice and the effects of the same chemotherapy on the patient-donors of the cell lines.

Answer 12:

Bibliographic Information

A phase III comparison trial of streptozotocin, mitomycin, and 5-fluorouracil with cisplatin, cytosine arabinoside, and caffeine in patients with advanced pancreatic carcinoma. Kelsen D; Hudis C; Niedzwiecki D; Dougherty J; Casper E; Botet J; Vinciguerra V; Rosenbluth R Department of Medicine, Memorial Sloan-Kettering Cancer Center, Cornell University Medical College, New York, New York Cancer (1991), 68(5), 965-9. Journal code:

0374236. ISSN:0008-543X. (CLINICAL TRIAL); (COMPARATIVE STUDY); Journal; Article; (JOURNAL ARTICLE); (MULTICENTER STUDY); (RANDOMIZED CONTROLLED TRIAL); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 1833042 AN 92005226 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Conventional chemotherapy for unresectable or metastatic adenocarcinoma of the pancreas has had little effect on palliation or survival. Almost all studies of systemic therapy have involved empiric use of a variety of Phase II or conventional agents alone or in combination. On the basis of recent studies using a human tumor pancreatic cancer (PC) xenograft in nude mice, a Phase I clinical trial of cisplatin, high-dose cytosine arabinoside (Ara-C), and caffeine (CAC) was performed in patients with advanced incurable PC. A tolerable dose and schedule of the three agents were developed. Seven of 18 patients with measurable disease in this Phase I trial had partial responses to CAC. A Phase III comparison of CAC versus standard treatment using streptozotocin, mitomycin, and 5-fluorouracil (SMF) was performed. Eighty-two patients with advanced PC were entered into this random assignment trial. The two treatment arms were well balanced for the usual prognostic factors. Although the acute (e.g., nausea and vomiting) toxicities of CAC were greater than those of SMF, both groups of patients tolerated treatment resonably well. Ninety percent of patients were evaluable for response. Two patients (5.5%) on the CAC treatment arm (95% confidence interval [CI], 0% to 15%) and four patients (10.2%) on the SMF treatment arm (95% CI, 1% to 22%) had objective responses (partial response in measurable disease or improvement in evaluable disease). No complete remissions were observed. The 95% confidence limits of response for CAC and SMF overlapped. The median duration of survival for all patients on the SMF treatment arm was 10 months, although it was 5 months on the CAC treatment arm (P = 0.008). In this Phase III comparison, CAC was not superior to conventional therapy with SMF in terms of response and was inferior for survival. Neither regimen is effective treatment for advanced PC.

Answer 13:

Bibliographic Information

The effect of the immune status of the TAR mouse on the growth and metastasis of tumour xenografts. Buckle A M; Goepel J R; Rees R C Department of Virology, University of Sheffield Medical School, U.K European journal of cancer & clinical oncology (1987), 23(6), 663-74. Journal code: 8112045. ISSN:0277-5379. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 3308478 AN 88004626 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Mice thymectomised at 3-4 weeks of age and subsequently given whole-body irradiation (9 Gy) under cytosine arabinoside cover (TAR mice) provide an alternative model to the athymic nude (nu+/nu+) mouse for studying the biological characteristics of tumour xenografts. In the present study we have evaluated the repopulation events in the bone marrow and spleen following whole body irradiation of TAR mice, and analysed immune competence up to 98 days following irradiation. Repopulation of both bone marrow and spleen was evident in the weeks following whole body irradiation, and an initial increase in the relative proportion of T-lymphocytes present in the spleen was followed by a decrease in the percentage of lymphocytes expressing T-cell markers, which remained below the level observed in control mouse spleen cell preparations. TAR mice exhibited a decreased ability to respond to a non-specific T-cell mitogen and to elicit a T-cell dependent antibody response to influenza viral antigen. Both TAR and control mice possessed macrophages which could be activated to the tumouricidal state, and natural killer activity of TAR mice was enhanced greater than 3-fold above control values. The ability of TAR mice to accept tumour xenografts decreased with the increasing time interval between irradiation and subcutaneous implantation of tumour cells, and (in some instances) spontaneous regression was observed. In addition, a hamster tumour cell line possessing high metastatic potential in its syngeneic host was shown to metastasise to the regional lymph node, lungs, liver, kidneys and spleen of TAR mice from a cell inoculum implanted subcutaneously immediately after irradiation; however, with increasing time between irradiation and inoculation of tumour cells tumour metastasis decreased. The ability of TAR mice to support the growth and metastasis of tumour xenografts would appear to inversely correlate with the increase in natural killer cell activity following irradiation

Answer 14:

Bibliographic Information

The growth and histological characteristics of a series of human bladder cancer xenografts. Hay J H; Busuttil A; Steel C M; Duncan W Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology (1986), 7(4), 331-40. Journal code: 8407192. ISSN:0167-8140. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 3809592 AN 87119126 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Xenografts from human transitional cell carcinoma of the bladder (TCC) have been successfully established in CBA mice which had previously been immune-deprived by thymectomy and whole body irradiation with cytosine arabinoside pre-treatment. Xenografts were established from 3/17 patients with histological grade 2 tumours, 3/19 patients with histological grade 3 tumours, and one from a patient with a mixed transitional cell and squamous cell carcinoma. No xenografts were established from patients with histological grade 1 tumours. All the xenografts maintained the histological characteristics of their parent tumours in early passage, but some developed more prominent squamous features in later generations. Many of the xenografts were cystic.

Answer 15:

Bibliographic Information

Sequential combination chemotherapy consisting of vincristine, peplomycin, methotrexate, cis-diamminedichloroplatinum (II), cytosine arabinoside and 5-fluorouracil, for advanced urothelial cancer. Yamauchi T; Hida S; Ooishi K; Okada K; Yoshida O Hinyokika kiyo. Acta urologica Japonica (1985), 31(7), 1093-104. Journal code: 0421145. ISSN:0018-1994. (CASE REPORTS); (ENGLISH ABSTRACT); Journal; Article; (JOURNAL ARTICLE) written in Japanese. PubMed ID 2414981 AN 86047350 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Two VPM-CisCF chemotherapy regimens (vincristine (VCR), peplomycin (PEP), methotrexate (MTX), cis-diamminedichloroplatinum (II) (CDDP), cytosine arabinoside (Ara-C) and 5-fluorouracil (5-FU), established using human bladder cancer xenografts in nude mice were applied for advanced urothelial cancer. VPM-CisCF (I) consisted of 0.4 mg/m2 VCR on days 1 and 4, 2 mg/m2 PEP on days 1-7, 2 mg/m2 MTX on days 2, 3, 5 and 6, 20 mg/m2 CDDP on days 8, 20 mg/m2 Ara-C on days 8 and 13, and 150 mg/m2 5-FU on days 10-12. VPM-CisCF (II) consisted of 0.6 mg/m2 VCR on days 1 and 3, 3 mg/m2 PEP on days 1-4, 3 mg/m2 MTX on days 2 and 3, 35 mg/m2 CDDP on day 4, 20 mg/m2 Ara-C on days 4 and 7, and 200 mg/m2 5-FU on days 5 and 6. These doses were adjusted for each case: the above mentioned dose x [(80/(40 + Age))2 + (Karnofsky's performance status/100)2]. VPM-CisCF (I) was administered to 6 patients (bladder cancer and transitional cell carcinoma), intra-arterially in two cases. One patient showed a complete response and survived for 7 months, three partial response (PR) surviving for 13, 8 and 37 (arterial-infused case) months, one showed minor response (MR) surviving for 4 months, and one had no change (NC) surviving for 5 months. VPM-CisCF (II) was administered to 11 patients (1 ureteral cancer, 1 renal pelvic cancer, 9 bladder cancer, and 10 transitional cell carcinoma except a case of mixed type of transitional cell carcinoma and squamous cell carcinoma). Four of the patients who had PR survived for 9, 8, 8 and 7 (alive) months, two who had MR survived for 8 and 4 months, three who had NC survived for 6, 4 and 4 months, and who two had progressive disease survived for 8 and 6 months. The major toxicities were myelosuppression and gastrointestinal symptoms, especially nausea and vomiting, but the treatment was well-tolerated.

Answer 16:

Bibliographic Information

Human tumour xenografts established and serially transplanted in mice immunologically deprived by thymectomy, cytosine arabinoside and whole-body irradiation. Selby P J; Thomas J M; Monaghan P; Sloane J; Peckham M J British journal of cancer (1980), 41(1), 52-61. Journal code: 0370635. ISSN:0007-0920. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 7362779 AN 80153850 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Mice immunologically deprived by thymectomy, cytosine arabinoside treatment and whole-body irradiation were used to study the growth of human tumours as xenografts. 10/16 melanoma biopsies, 4/13 ovarian carcinoma biopsies and 3/6 uterine cancer biopsies grew as serially transplantable xenograft lines. The tumour lines were studied through serial passages by histology, histochemistry, electron microscopy, chromosome analysis, immune fluorescence, growth rate measurement and mitotic counts. They retained the characteristics of the tumours of origin, with the exception of loss of pigmentation in two melanomas, histological dedifferentiation in the uterine carcinomas, and increased mitotic frequency and growth rate in some melanomas. It was concluded that this type of animal preparation is as useful as alternative methods of immunological deprivation, or as athymic nude mice, for the growth of human tumour xenografts, at least for some experimental purposes.